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## **THE DIAGNOSIS OF HEREDITARY ANGIOEDEMA: FAMILY CAREGIVERS' EXPERIENCES.**

Granero-Molina, J., Sánchez-Hernández, F., Fernández-Sola, C., Jimenez-Lasserrotte, MM., Antequera-Raynal, LH., Hernández-Padilla, JM. (2018) The Diagnosis of Hereditary Angioedema: Family Caregivers' Experiences. *Clinical Nursing Research*. (Published online first). DOI: <https://doi.org/10.1177/1054773818780102>

### **Abstract**

The aim of this study was to understand the experiences of family caregivers in the process of diagnosing hereditary angioedema. An interpretive and qualitative research methodology based on Gadamer's philosophical hermeneutics was carried out. Data collection took place between May 2015 and August 2016 and included a focus group and in-depth interviews with 16 family caregivers. Two themes define the experiences of family caregivers: 'Family life focuses on identifying the problem' and 'Discovering and coping with a complex diagnosis'. The process of diagnosis generates fear, anxiety, uncertainty and incomprehension. Family caregivers are the main support for patients diagnosed with hereditary angioedema. As they share in the patients' suffering, they need a diagnosis to be established in order to be able to cope with the disease and offer support. Family health nurses can contribute to improving the coping process in this phase of the disease.

### **Keywords**

Hereditary angioedema, family caregivers, rare diseases, phenomenology

## **Introduction**

Hereditary angioedema due to C1 inhibitor deficiency (HAE) is a genetic condition caused by a decreased synthesis or functionality of the C1 esterase inhibitor (C1INH) (Triggianese et al., 2015). HAE is considered a rare disease and its worldwide prevalence varies between 1:10,000 and 1:50,000 (Caballero et al., 2013; Li et al., 2015). In Spain, a prevalence of 1.09 cases/100,000 inhabitants has been reported (Prior et al., 2012). Currently, HAE is considered to be an under-diagnosed condition that can be unknown to doctors, nurses and other healthcare professionals (Otani et al., 2017). Furthermore, the management of HAE in clinical practice varies depending on whether or not patients remain asymptomatic or suffer sudden, recurrent, unpredictable and life-threatening attacks (Prior et al., 2012).

HAE can be associated with physical symptoms such as skin, gastrointestinal and respiratory edema (Betschel et al., 2014), pain, diarrhea and vomiting (Hofman et al., 2016). It can also cause psychological disorders such as fear, anxiety and depression (Macginnitie, 2014). HAE is difficult to diagnose and the specific treatment options are limited (Li et al., 2015), which added to the sudden nature of the attacks, can affect people's quality of life throughout all stages of the disease (Prior et al., 2015). The effects of HAE on patients' lifestyle and biopsychosocial health also affect their family caregivers (Bygum et al., 2015). Although HAE has been studied in families at the clinical, immunological and hereditary level (Triggianese et al., 2015), the experience of family caregivers during the diagnostic process has not been fully explored yet.

## **Background**

HAE is a hereditary disease of a dominant autosomal nature. A child whose mother or father suffers from HAE has a 50% chance of suffering from it too. HAE is classified into Type I (80-85% of cases, low levels of C1INH and reduced functionality) and Type II (15-20% of

cases, normal or elevated levels of C1INH and low functionality) (Bonner et al., 2015; Hofman et al., 2016; Sánchez et al., 2015; Triggianese et al., 2015). HAE episodes are characterized by subcutaneous edema in the skin, the gastrointestinal tract and the upper respiratory tract (Betschel et al., 2014; Bygum et al., 2015; Lasek-Bal, Holecki, Handzlik-Orlik, Smertka, & Duława, 2015). This can cause disfiguration, pain and difficulties in carrying out daily living activities (Bygum et al., 2015; Gomide et al., 2013; Lumry, Miller, Newcomer, Fitts, & Dayno, 2014). Patients may also experience spasms, colic pain, vomiting and diarrhea. (Hofman et al., 2016; Macginnitie, 2014). The main cause of HAE mortality is the obstruction of the upper respiratory tract by laryngeal edema (Arkuszewski, Meissner, & Szram, 2015; Longhurst et al., 2016; MacBeth, Volcheck, Sprung, & Weingarten, 2016). In patients diagnosed with HAE, physical symptoms are often associated with psychological problems such as depression or anxiety (Aabom, Andersen, Perez-Fernández, Caballero, & Bygum, 2015; Valle, França, Campos, & Sevciovic, 2011) hence the need for exploring corporality disorders, stigma (Sánchez et al., 2015), self-management (Bonner et al., 2015), coping mechanisms and social and family support (Aygören-Pürsün et al., 2014).

Although research on rare diseases has traditionally focused on patients' experiences, HAE also affects family caregivers (Årestedt, Persson, & Benzein, 2014; Deek et al., 2016; Rosland & Piette, 2010). Throughout the whole disease process, patients share experiences of symptoms, risks, treatment, self-care and healthcare demands with their family caregivers (Årestedt, Benzein, & Persson, 2015; Cicardi et al., 2012; Rosland & Piette, 2010).

Therefore, family caregivers constitute a fundamental source of support for the effective management of HAE (Bott, Kapp, Johnson, & Magno, 2009). Offering such support implies having to deal with the visual impact of the sudden swelling attacks, deciding when it is appropriate to seek medical help, administering an injection in life-threatening situations, and taking on additional responsibilities at home (Bygum et al., 2015). Additionally, until the

final diagnosis is established, family caregivers go through a long search process (Jaradat et al., 2016) in which they have to learn to recognise the symptoms of HAE (Rosland, Heisler, & Piette, 2012) and to effectively manage emotions and social relationships (Dos Santos, Santos, & De Montigny, 2015). As a consequence, family caregivers may experience negative feelings such as stress or guilt (Longhurst & Bygum, 2016), which, in turn, can compromise the quality of life of both patients and relatives (Caballero et al., 2014; Prior et al., 2015). However, despite the physical, psychological and social burden associated with this chronic condition (Dos Santos et al., 2015; Silibello et al., 2016), family caregivers' needs and experiences can go unnoticed (Greenwood, Mackenzie, Cloud, & Wilson, 2010). Although some studies have focused on exploring the relationship between doctors and family caregivers as well as their experiences in the emergency department triage, (Caballero et al., 2014; Lane, Grant & Dougherty, 2012), our literature review shows a scarcity of evidence on family caregivers' experiences during the HAE diagnosis process. Understanding the way they experience this process can help patients and caregivers to develop adaptation strategies, benefit from mutual support, learn to make appropriate use of the resources and cope with the situation (Årestedt et al., 2014; Silibello et al., 2016; Zurynski et al., 2017).

The Family Management Style Framework (FMSF) allows us to conceptualize how family members incorporate managing a chronic disease into the context of their daily lives (Knafl & Deatrick, 2003; Knafl, Deatrick, & Gallo, 2008; Knafl, Deatrick, & Havill, 2012). The three adapted components of the FMSF include: *Definition of the situation surrounding care* (how the caregiver defines the family member with HAE's illness, vulnerabilities and capacities), *The management of care* (goals and philosophy that guide the caregivers' in their role and responsibilities of caring for the family member with HAE), and *Perceived consequences of care* (impact of HAE patient care on family expectations, trajectory and

functioning). The aim of this study was to understand the experiences of family caregivers in the process of diagnosing HAE.

## **Methods**

### **Study Design**

A qualitative approach based on Gadamer's hermeneutic phenomenology was employed in the processes of data interpretation and analysis (Gadamer, 2005). According to Gadamer's philosophy, human understanding is an interpretive process, which implies a dialogue between the interpreter and the text (or transcription) in a fusion of horizons. Understanding a phenomenon involves acknowledging the present time, our culture and our history (Gadamer 2005, p. 360-377).

### **Participants**

Through convenience sampling, family caregivers of HAE patients were selected. Inclusion criteria were: to be a direct family member and caregiver (father, mother, sibling, offspring or partner) of the patient, to live together or to have lived together for more than 5 years and for the patient to have had more than 2 HAE attacks in the last year. The exclusion criteria were: to refuse to participate in the study and to have been diagnosed with HAE.

### **Data collection**

The study took place in an association of HAE patients. Data collection included a focus group (FG) and in-depth interviews (DI) and it was completed between May 2015 and August 2016. HAE is a rare disease with a large geographical dispersion. The FG was comprised of family caregivers who accepted to discuss and share their experiences about the diagnosis process with other participants. DIs were carried out with those family caregivers who preferred not to share or discuss their experiences with other participants. The FG was comprised of six participants, it had a duration of 57 minutes and it started with the question: *"Can you tell us about your experiences as a family caregiver of a patient diagnosed with*

*HAE?*” and ended with the question “*Is there anything else you would like to add on the topic?*” Subsequently, 10 in-depth interviews were completed, which allowed for the exploration of emerging themes. All of the interviews were individual, private and lasted an average of 40 minutes. Socio-demographic data of the participants were collected before commencing the interviews. All of the participant responses from the FG and DIs were audio-recorded and transcribed (Green & Thorogood, 2014). The transcriptions were included in a hermeneutic unit and analysed using the software Atlas-ti 7.0. The data collection through interviews were stopped when data saturation was reached.

### **Data Analysis**

A modified form of the stages developed by Fleming, Gaidys, & Robb (2003) was used. In the first step, the relevance of the research question was assessed and the researchers answered the following question affirmatively: ‘*Can the experiences of family caregivers of HAE patients be studied from the phenomenological hermeneutics?*’ The second step was for the researchers to reflect upon their pre-understanding of the disease. One researcher is an HAE patient, while the rest have investigated experiences in chronic diseases. The third step aimed to achieve an in-depth understanding of the phenomenon through dialogue between the researcher and the participants. The researchers verified that the FG and DI data describe the experiences of family caregivers of patients with HAE. New questions emerged such as, ‘*What role does the family play in the self-care of the patient with HAE?*’ The fourth step aimed to understand the phenomenon through dialogue with the text. After reading the transcriptions, the participants’ experiences were re-examined together with the researchers’ horizons and new questions such as ‘*What influence does the hereditary nature of HAE have on the family?*’ All transcriptions were analysed line by line to reveal the quotes that contributed to the understanding of the phenomenon. Three members of the research team independently performed the data coding. Then, all their interpretations were compared

amongst them. If the researchers did not agree on a particular unit of meaning, subtheme or theme, this was excluded from the analysis and a more appropriate one was found. The study's themes, sub-themes and units of meaning can be seen in Table 2. Only the most relevant quotes were selected by consensus to be included in the study. In the fifth stage, reliability and rigor of the qualitative data was established. To increase trustworthiness, three researchers analyzed the data separately, discussing the differences until they reached an agreement. Recordings, data analysis and interviews were saved to guarantee dependability. Participants validated the transcription and data analysis. Participants with extensive experience in caring for patients diagnosed with HAE were selected.

### **Ethical considerations**

Patients were contacted to request their relatives' participation. All participants were informed of the study's aim and the voluntary nature of their participation. They also signed an informed consent form before participating. Furthermore, participants were asked for permission to record the conversations and were given access to the results of the study. In order to ensure confidentiality and anonymity, all interviews were given codes. Approval was obtained from the university's Ethics and Research Committee (Number: 25/2017).

### **Results**

The final sample was comprised of 16 family caregivers. Their average age was 45.19 years ( $SD = \pm 12.38$ ; range = 27-67) and the average time passed since their relative had been diagnosed with HAE was 27.87 years. The participants' characteristics are provided in Table 1. Two themes, together with their subthemes and units of meaning, allow the experiences of family caregivers in the process of diagnosing HAE to be understood (Table 2).



**Table 1***Socio-demographic data of the participants (N=16)*

| Participant | Sex    | Age | HAE(years) | Relationship |
|-------------|--------|-----|------------|--------------|
| DI1         | Male   | 27  | 9          | Brother      |
| DI2         | Female | 28  | 12         | Sister       |
| DI3         | Female | 32  | 15         | Daughter     |
| DI4         | Female | 35  | 7          | Wife         |
| DI5         | Male   | 37  | 14         | Husband      |
| DI6         | Female | 42  | 20         | Daughter     |
| DI7         | Female | 44  | 24         | Wife         |
| DI8         | Female | 55  | 33         | Aunt         |
| DI9         | Female | 56  | 32         | Wife         |
| DI10        | Female | 67  | 48         | Mother       |
| FG1         | Female | 34  | 3          | Mother       |
| FG2         | Female | 46  | 4          | Mother       |
| FG3         | Female | 49  | 30         | Wife         |
| FG4         | Male   | 51  | 26         | Father       |
| FG5         | Male   | 57  | 33         | Husband      |
| FG6         | Male   | 63  | 40         | Father       |

**Note.** DI = In-depth interview. FG = Focus group

**Table 2***Themes, subthemes and units of meaning.*

| Theme   | Subtheme   | Units of meaning   |
|---|--|--|
| Family life focuses on identifying the problem. | The exhausting beginning of an unknown disease: a torturous road to diagnosis.     | Lack of specificity. Indescribable. Unpredictable. Incomprehension. Anguish, despair and bewilderment. The need to know. Minimizing importance. Wasting time. Pilgrimage in search of treatment. |
|   | Living on a knife-edge.  | Fear, insecurity. Rescue medication. Enduring the HAE attacks. Openness and transparency.  |
|   | Between the professionals' lack of knowledge and the stigmatization of the family. | My son does not swell up because I am crazy. Lack of medical knowledge. Unnecessary interventions. Race against time.  |
|   | Managing HAE within family life.   | Relief. Blood ties. The need for care. They are special people. Stigma.  |

**Family life focuses on identifying the problem**

This theme describes the experiences of family caregivers at the outset of HAE, the vulnerability of the patient and their responsibility in caring for their relative. From the manifestation of the first symptoms, caregivers are immersed in a long, unknown process. They are confused and need to give the problem a label and obtain a final diagnosis.

***The exhausting beginning of an unknown disease: a torturous road to diagnosis.***

The participants recognize their concern and they know that something is happening but they cannot find words to define it. HAE starts with nonspecific symptoms and an unpredictable course. For patients and caregivers, ‘not knowing’ affects how they internalize the disease. Family caregivers need to make sense of the new situation and focus on their ability to look after their relative. They need to know what the causes and the severity of the disease are so that they can understand how vulnerable the patient is. However, this is difficult to achieve and they often do not know how to describe what is happening to them. They are faced with the incomprehension of other relatives, friends, neighbours and healthcare professionals.

*At first you think about a million things, little by little you see that it's different, strange... (It's) difficult to understand if you haven't gone through it. You don't know how to describe it and that's why they don't understand you. (D11)*

Although HAE causes patients to experience pain, body image disorders and loss of social relationships, their family caregivers tend to conceptualize the disease as a threat to life that reduces quality of life considerably. The unpredictability of the crises keeps patients and caregivers on alert, which is exhausting. They continuously worry about their ability to effectively manage care and comply with the treatment recommendations. As one participant describes it, the non-specificity of the triggers and the magnitude of the risks prevent patients and caregivers from carrying out their daily living activities at ease.

*You don't know when or how it will come. It's a constant and profound concern that puts limitations on our daily lives...especially psychologically. (FG5)*

As a result of living with and caring for patients diagnosed with HAE, family caregivers experience feelings of anguish, despair and bewilderment. In addition, continuous visits to the emergency department, hospital admissions, and mistakes in the diagnosis process lead to physical and psychological exhaustion. Family caregivers start disagreeing on

what the severity of the disease is and the way in which it should be handled. This results in a negative dynamic in the ‘*parental mutuality*’, causing emotional instability and making it more difficult to effectively manage and cope with care.

*I don't handle it well, it fills me with anguish and it gets worse. You can't forget everything that we have gone through. In the end you feel relieved, ... but you are exhausted.* (DI4)

Establishing HAE diagnosis is a complex process that can take years. Patients and family caregivers often go through erroneous treatments and unnecessary surgeries. Healthcare professionals tend to underestimate the importance of the problem, attributing the symptoms to common diseases. Family caregivers experience these errors as a waste of time, which leads to a lack of trust in healthcare professionals.

*After 6 or 7 hours in the emergency room, the doctor said that an insect must have bitten him. I said no, this has happened to him many times and it isn't an insect bite, and he told me: Go home, this is no emergency.* (DI9)

Family caregivers feel neglected, vulnerable and incapable of managing the situation. They are bewildered when, for example, a hand inflammation leads to meetings of medical teams and after a long wait, they prescribe ineffective treatments or refer the patient to another hospital. In these situations, they continue to be unaware of what they are facing. As a participant says, patients and family caregivers wander from one healthcare centre to another on a pilgrimage that diminishes their quality of life.

*One night the middle of his throat swelled up (it had never happened). We went back to the hospital and they told us: I won't give you anything else. I don't know what you have. I'll send you to the other hospital and they'll look at you there.* (DI7)

While patients are subjected to a wide variety of generally ineffective treatments, caregivers' goals, priorities and expectations are continuously modified.

*They told us that when his feet were swollen we should put them in cold water, to keep them there for a little while, then put them in hot water and leave them for another short time. They gave us explanations of all kinds but none were valuable. (FG6)*

### ***Living on a knife-edge.***

The progression of HAE gradually increases the anguish levels amongst caregivers. At the core of their concerns is the unpredictability of the attacks and the inability to help patients. Family caregivers fear the painful and disabling episodes; however, they especially fear the edemas, which vary between a simple skin edema and a life-threatening edema of the upper respiratory tract. These fears affect the way patients and caregivers see life. As a participant says, although life continues, it is like living on the edge of the abyss.

*The two words that define HAE are anguish and fear. You live with that feeling, you go to bed with the fear of what could happen that night, you wake up with the uncertainty of whether everything is going to be ok... (FG4)*

As a rare disease, HAE bewilders the patient, family and healthcare professionals. After the manifestation of the first symptoms, family caregivers accompany patients to various hospitals looking for a diagnosis. Participants describe the disbelief and astonishment of the medical teams towards something they have not seen before. For patients and caregivers, this is a source of insecurity and uncertainty.

*Once his hand swelled up quite a lot, we took him to the hospital and there, 4 doctors stared, amazed, did not know what to do or say ... but we had seen these episodes many times. (DI6)*

Family caregivers voiced feelings of devastation. Some have lost a family member to an HAE attack or have a relative who needed an emergency tracheotomy. Caregivers feel that the difficulty in establishing the diagnosis and the limited attention paid by doctors to what they have to say lead them to experiencing extreme situations.

*We had been begging them for hours to listen to us. We knew that the adrenaline and corticosteroids were not going to work, it was becoming harder for him to talk, it was hard for him to swallow, and even so they preferred to wait to see how it evolved before administering C1 because they had never administered it to him before and they feared a reaction. But he was choking! We thought they would have to open his trachea for him to breathe, it was horrible. (DI8)*

From the onset of HAE, the way family caregivers approach the management of the disease focuses on not hiding it in daily life situations. Family caregivers integrate patient care into the rest of their family commitments. Given its hereditary nature, they may have coexisted with HAE in previous generations and this facilitates coping with the disease.

*I have always talked about it openly to classmates and teachers. If she has to go to school and her foot is swollen, she'll just wear slippers... Is she going to hide it?*

(FG1)

Nevertheless, until the final diagnosis is established, family caregivers are never fully satisfied with the way the situation is managed. They continuously wonder what the problem and its solution might be.

*What are you facing? I knew there had to be some explanation, that someone would tell me what was going on to know what the next step was. Because if you don't know what the problem is called you can't face it nor seek help or a solution. (DI5)*

### **Discovering and coping with a complex diagnosis**

This theme describes the experiences of family caregivers regarding the process of establishing a diagnosis, the relationship with healthcare professionals and the initial consequences of the diagnosis on personal and family life.

***Between the professionals' lack of knowledge and the stigmatization of the family.***

Doctors can confuse HAE symptoms with other diseases. This can lead to establishing an erroneous diagnosis that, in turn, can be the cause of patients suffering pain and undergoing unnecessary surgical interventions. Family caregivers worry about the patient and feel that the situation is out of their control. The delay in establishing the correct diagnosis and the inadequacy of the prescribed treatments not only increase the length of the attacks but also the levels of anxiety in patients and caregivers.

*When his hands or feet were swollen it was rheumatism, when the intestine was unwell it was gastritis. If it was colic pain, (then it was) appendicitis. They told him to eat light, removed the appendix and he remained the same. They didn't know what it was but it was too late. (DI3)*

For family caregivers, the diagnosis is a never-ending process that causes them to feel guilty and responsible for what happens to their relative. The delay in HAE diagnosis implies seeing relatives suffering from attacks and undergoing invasive procedures for diagnostic tests. This situation affects the family, who face it as a struggle and a race against time.

*Since we didn't know what she had, we spent many years unable to enjoy ourselves as a family. (We were) always worried. We were lost, not knowing what it was or if something was going to happen to her ... it was no way to live. (DI2)*

Ignorance about HAE generates bewilderment amongst healthcare professionals, who question the veracity of testimonies from patients and relatives about symptoms, crises or previous treatments. Family caregivers can relate the attacks with triggers such as physical activity, stress, falls or hormonal changes. For them, more awareness about HAE is needed amongst healthcare professionals. This would stop the anguish of family caregivers from being misinterpreted or confused with mental health disorders by healthcare professionals.

*They sent me to the psychiatrist and I told (the doctor): listen, my son doesn't swell up at 6 o'clock in the morning because I'm crazy. (DI10)*

***Managing HAE within family life.***

The establishment of a final diagnosis changes the family's focus and expectations. They start integrating their HAE '*management approach*' into their family routines. Caregivers feel relieved when they receive the final diagnosis. The diagnosis opens up the possibility of feeling protected by medication and being able to explain what has been happening to their relative. They start to understand their limitations (i.e. not being able to get out of bed, not being able to go to work or school etc.) and find people who suffer from the same condition. Patient associations are a fundamental source of support for patients and caregivers. They help them to understand more about the disease, to share concerns and to offer mutual help.

*When I was told the diagnosis, it was a relief to know that there was medication and an association of patients with the same problem to share experiences. (FG3)*

They also express relief regarding their environment because HAE is a rare disease that people around them could not understand and which they can now explain. The establishment of an HAE diagnosis also improves understanding amongst healthcare professionals. Patients and family caregivers do not only improve the way they manage physical symptoms but they also stop feeling misunderstood, intimidated and stigmatized.

*What I felt after the diagnosis was relief, knowing I wasn't crazy. (DI10)*

The genetic nature of the disease can facilitate the diagnosis. Many families have been diagnosed thanks to other relatives also being diagnosed and some parents have been diagnosed because their children were diagnosed first. Faced with the symptomatic coincidence, patients and relatives suggest the diagnosis to the doctors, which prompts earlier genetic studies and early treatment.

*We ran into a cousin of hers and when we told her about the symptoms she said: Oh! I know what you have...and thanks to that she was diagnosed. (DI5)*



From the first manifestation of symptoms, the family is brought together around the patient and he/she becomes the main object of care. During the search for a diagnosis, family caregivers find themselves in a stressful situation that causes them to neglect their own needs. When families face HAE, the whole group is restructured and priorities are redirected. It is usually the mothers who assume the role of main family caregiver. They may quit their jobs, minimize their leisure time, and even neglect other family members. This forces the rest of the family to take on new responsibilities as well as to restructure their expectations and future plans (i.e. considering changing jobs, accounting for new expenses, learning how to administer drugs, having to pay continuous visits to healthcare centres, etc.). Ineffective coping with this situation may lead to incomplete adaptive processes.

*People around them are not patients, but they are affected ... we suffer as much as they do. It was dreadful for me to see him suffer so much, I could not abandon him at home and leave. I left my job to be closer to him when he needed me. (DI9)*

Family caregivers develop deep-rooted empathy with HAE patients. They describe them as "special people" and admire their resilience to pain, dehydration, fainting and suffering. However, they also worry about the impact that social stigma may have on patients' social lives. They express feeling psychological pain and existential anguish because they fear their relatives could struggle, for example, to find a partner (*'people may not accept their condition'*), to have children (*'they could inherit the disease'*), and to succeed academically and professionally (*'due to having frequent crises'*). Family caregivers fear patients will not be able to fulfil their goals in life. As one of the participants says, "they are special" but it is very difficult to be the main caregiver and pay attention to the needs of the rest of the family.

*They have a strength and a capacity for suffering that the rest (of us) don't have; their pain threshold (physical, psychological and existential) is much higher. (FG4)*

## **Discussion**

The purpose of this study was to understand the experiences of family caregivers in the process of diagnosing HAE. The adapted FMSF used in this study provided a framework for understanding the impact of the process of diagnosing HAE on the family and the changing roles and responsibilities of the caregiver. The three components of the FMSF (Knafl & Deatrick, 2003; Knafl et al., 2008; Knafl et al., 2012) and their associated dimensions identify strengths, weaknesses and family management styles of the disease. Multiple studies analyze HAE from an epidemiological (Riedl, 2012), immunological (Triggianese et al., 2015), socio-economic (Aygören-Pürsün et al., 2014) or pharmacological perspective (Longhurst et al., 2016). However, there is little research focusing on the experiences of patients and relatives (Bygum et al., 2015). According to our results, from the onset of the first symptoms families experience the problem together with the patient. Nonetheless, they need to give a name to a situation they do not understand. As with other chronic diseases (Årestedt et al., 2015), a complex diagnosis prolonged over time has devastating effects on the family (Anderson, Elliott, & Zurynski, 2013; Garrino et al., 2015). The lack of specific symptoms and the unpredictability of the attacks submerges the family in anguish, despair and bewilderment (Årestedt et al., 2015). We concur with Bygum et al. (2015) in that the vulnerability of the patient generates fear, insecurity and concern in the family. The absence of a diagnosis masks the risks and the development of HAE (Dos Santos et al., 2015; Michalík, 2014), making the adaptation process more difficult for the family.

As with other studies of caregivers (Anderson et al., 2013; Michalík, 2014), our participants define HAE by their negative experiences (Garrino et al., 2015). Studies of patients and families indicate anxiety (Dos Santos et al., 2015; Sánchez et al., 2015), fear and grief (Aabom et al., 2015; Caballero et al., 2013). The absence of a diagnosis, the HAE attacks, and dependence on medication can generate stress (Craig et al., 2012; Greenwood et

al., 2010), problems managing the therapeutic regimen and difficulty in family adaptation (Cicardi et al., 2012). A wide view of strengths and weaknesses is key in adapting family management styles (Knafl et al., 2008) and the first step is doing everyday activities in a natural way (Bygum et al., 2015). The management of behaviors involves a consensus on the goals, priorities and management of HAE at the family level (Michalik, 2014). The difficult road to diagnosis requires incorporating HAE into everyday life routines (Betschel et al., 2014; Deek et al., 2016), coming to terms with the trivialization of healthcare services and accompanying the patient (Arkuszewski et al., 2015). According to our results, HAE affects the quality of life of patients and families (Aabom et al., 2015; Bygum et al., 2015; Deek et al., 2016; Silibello et al., 2016). Family caregivers develop psychological problems, as well as complex and unknown needs (Årestedt et al., 2015; Caballero et al., 2014; Jaradat et al., 2016). The perceived consequences begin with the need to know (Årestedt et al., 2014); the family member focuses on conveying their feelings with openness. We agree with Lane et al. (2012) on the deleterious consequences on patients and families of not recognizing this disorder. In addition, our caregivers emphasize that they suffer fear, helplessness and stigma when faced with healthcare professionals' lack of knowledge and unwillingness to listen. As in our study, the phase of diagnosis is slow and painful (Caballero et al., 2013; Macginnitie, 2014). The balance between the caregiving role, one's personal life and the adequacy of future expectations are fundamental for adaptation (Greenwood et al., 2010; Silibello et al., 2016). No differences in future concerns related to the diagnosis were found but our participants start making sense of their new situation when they discover the existence of medication for the symptoms and when they contact other patients and associations (Bygum et al., 2015). Some studies connect HAE and depression in patients (Riedl, 2012; Valle et al., 2011), a matter to be studied in family caregivers. We agree with Cipolletta, Marchesin, & Benini (2015) in the need for care, healthcare and social support for these families. Caring for

a patient with HAE implies a sudden change for family caregivers and constitutes a difficult life experience (Michalík, 2014). From the very first symptoms, the delays in diagnosis and the lack of support (Anderson et al., 2013) fall within the remit of a family health nurse's area of care.

### **Limitations**

In Spain, the provision of healthcare services varies across regions. Consequently, including participants from different regions could yield different results. Our participants were all white-Spanish and there were very little variability in their socioeconomic backgrounds. Recruiting participants from different races and socioeconomic backgrounds could lead to different results. HAE is a rare disease and family caregivers fear being recognized in the text. One of the authors stated being diagnosed with HAE and his experiences could have influenced the data interpretation. Future research should include the experiences of patients and healthcare professionals.

### **Conclusion**

HAE is a rare chronic disease of hereditary nature with devastating effects on the lives of patients and their families. Although there are asymptomatic phases, the outbreaks are accompanied by pain, inflammation, disability, and risk of suffocation by laryngeal edema. Although immunological or pharmacological research has reported important advances, this study stems from the need to explore the experiences of patients and families from the onset of the first symptoms. Family caregivers have reported that the delay in receiving a diagnosis generates fear, anxiety, uncertainty, ignorance, isolation and incomprehension. Family caregivers, being involved in all phases of the diagnostic process, require attention, credibility and for doctors and healthcare professionals to listen to them. This could improve the understanding and awareness of HAE as well as patients' and families' suffering. It could also favor earlier diagnosis, avoiding unnecessary interventions. Since the family caregivers

are the first line of support to these patients, they also need to define the problem, know what the diagnosis is and adapt disease management to family functioning, relationships and routines. Knowing the experiences of families can help detect needs, improve decision-making or reduce stigma. Family health nurses can help enhance knowledge, assist in the process of searching for a diagnosis or train patients and family caregivers to administer medication and support care needs.

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### **Declaration of Conflicting Interests**

The authors declared no potential conflicts of interest.

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